UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/334,325	06/16/1999	STEWART A. CEDERHOLM-WILLIAMS	CV0276A	5209

7590 09/08/2003

T R FURMAN
BRISTOL-MYERS SQUIBB COMPANY
100 HEADQUARTERS PARK DRIVE
SKILLMAN, NJ 08558

EXAMINER
CHEN, SHIN LIN

ART UNIT	PAPER NUMBER
1632	25

DATE MAILED: 09/08/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/334,325	CEDERHOLM-WILLIAMS, STEWART A.	
	Examiner	Art Unit	
	Shin-Lin Chen	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 June 2003 and 18 June 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 13-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 13-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☐ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other:

DETAILED ACTION

Applicant's amendments filed 6-16-03 and 6-18-03 have been entered. Claim 2 has been canceled. Claim 17 has been added. Claim 1 has been amended. Claims 1 and 13-17 are pending and under consideration.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1 and 13-16 remain rejected and claim 17 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of transforming a cell *in vivo* as taught by Donovan et al., 1998 (US Patent No. 5,833,651), does not reasonably provide enablement for a method of transforming a cell *in vivo* by applying a nucleic acid and a pliable, adhesive fibrin gel to said cell with apparatus other than stent or balloon catheter. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims and is repeated for the reasons set forth in the preceding Official action mailed 3-12-03 (Paper No. 22).

Applicant's arguments filed 6-16-03 have been fully considered but they are not persuasive.

Applicant argues that the claims are not directed to gene therapy but rather are directed to transforming a cell, which is not unpredictable (amendment filed 6-16-03, p. 2). This it not found persuasive because of the reasons set forth in the preceding Official action mailed 3-12-03 (Paper No. 22). The claims read on applying a nucleic acid to cells in vivo so as to transform

cells and the transformation of cells in vivo must have a use, which is to provide therapeutic effect in vivo. The title of the present invention reads "Fibrin sealant as a transfection /transformation vehicle for gene therapy". Therefore, the claims read on gene therapy in vivo, which is unpredictable at the time of the invention. Further, the specification fails to provide adequate guidance and evidence for how to administer a pliable, adhesive fibrin gel either mixed with a nucleic acid or separate from a nucleic acid to a subject such that target cells in said subject are transformed with said nucleic acid. The specification also fails to provide adequate guidance what apparatus is used to deliver the pliable, adhesive fibrin gel to target cells in a subject for transformation of said cells where the pliable, adhesive fibrin gel will polymerize quickly. There is no evidence of record that shows transformation of target cells in a subject with any nucleic acid via administering the pliable, adhesive fibrin gel and the nucleic acid in a mixture or administering said fibrin gel and nucleic acid in a sequential order. Thus, claims 1 and 13-16 remain rejected and claim 17 is rejected under 35 U.S.C. 112 first paragraph.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002

do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 17 is rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Donovan, 1998 (US patent No. 5,833,651) and is repeated for the reasons set forth in the preceding Official action mailed 3-12-03 (Paper No. 22). Applicant's arguments filed 6-16-03 have been fully considered but they are not persuasive.

The newly added claim 17 is an independent form of the original claim 2, which reads on mixing the nucleic acid and a fibrin or fibrinogen composition before applying to the cells.

Applicant argues that Donovan does not suggest entrap nucleic acid in a pliable fibrin gel adhered to a cell (amendment, p. 3). This it not found persuasive because of the reasons set forth in the preceding Official action mailed 3-12-03 (Paper No. 22). Donovan teaches a method for delivering nucleic acid to cells accessible from a wall of a body lumen comprising providing a stent having a lumen-wall contacting surface, a lumen-exposed surface, a first polymer composition comprising fibrin covering at least a portion of the lumen-wall contacting surface to form a polymer covered stent, and a virus to deliver nucleic acid to a cell wherein the virus is

associated with the first polymer composition covering the lumen-wall contacting surface, and positioning said stent in a lumen of the body to deliver said nucleic acid to said cell (e.g. column 3, 4, 20). Donovan also teaches mixing a solution of fibrin monomer and virus containing nucleic acid to form a polymer, i.e. fibrin gel, which can be used to deliver the virus to the cell, and suggests the polymer composition comprising fibrin and virus provide a unique stabilizing composition for gene delivery (e.g. column 13, lines 9-12, 64, 65). Therefore, one of ordinary skill at the time of the invention would have been motivated to mix a nucleic acid and a fibrin composition to form a pliable adhesive fibrin gel for gene delivery with reasonable expectation of success.

Conclusion

No claim is allowed.

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shin-Lin Chen whose telephone number is (703) 305-1678. The examiner can normally be reached on Monday to Friday from 9:30 am to 6 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds can be reached on (703) 305-4051. The fax phone number for this group is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is (703) 308-0196.

Shin-Lin Chen, Ph.D.

S/Chen